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TECHNICAL NOTE

Effect of membrane grain orientation on *in vitro* performance of a Kiil dialyzer

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The membranes used almost exclusively in artificial kidneys are cellophane and Cuprophan. In both, the polymer chains are arranged preferentially, though not completely, in the direction of extrusion. The physical properties of these microporous membranes have been extensively investigated [1, 2], and it has been shown [3] that the pores of these membranes are rather irregular but preferentially elliptical, with the greater diameter in the direction of extrusion. The effect, however, of grain orientation on their behavior during hemodialysis has not been reported. The problem is particularly important in the case of the Kiil dialyzer (Fig. 1), the most popular type in use, in which the membrane support consists of a number of V-shaped grooves lying parallel to the direction of flow of blood and dialysis fluid. The dialyzer is assembled in hospital or home using sheets of Cuprophan, or cellophane, which are available with the grain parallel to the grooves ("long grain") or at right angles to them ("cross grain"); the choice at the moment depends on the whim of the physician. On behalf of the U.K. Department of Health and Social Security we have therefore investigated the effect of grain orientation on the performance characteristics of a Kiil dialyzer. A full report on this work is available on request [4].

A standard two-layer Watson Marlow Kiil was assembled on 26 occasions, alternating with cross-grain and long-grain cuprophan membranes supplied by Bemberg Folien GmbH, Wuppertal, West Germany. Ten of the comparisons were made by cutting the two orientations from a batch of square membrane sheets supplied by the manufacturer as standard material. In the remainder the membranes came from different batches of the standard rectangular sheets supplied to dialysis units. Standard

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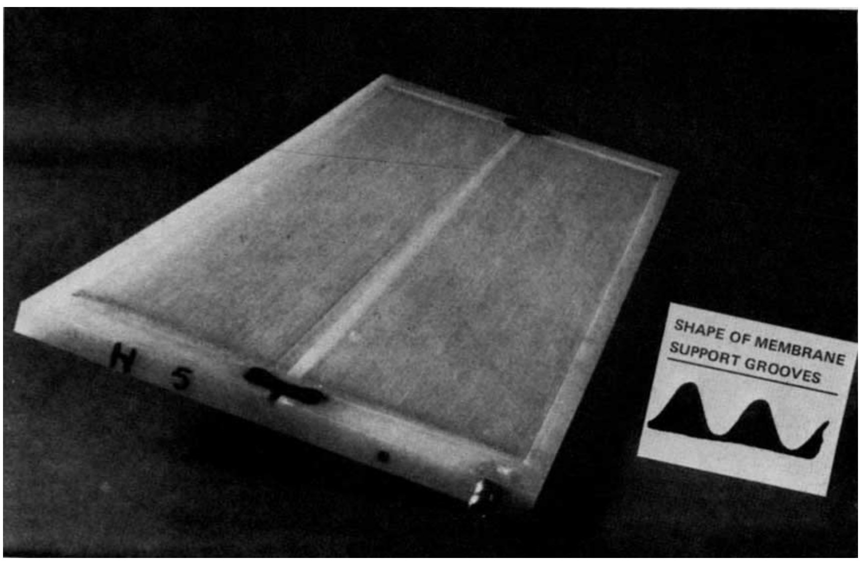

Fig. 1. *Single Kiil board with longitudinal grooving.* (Inset shows cross section of grooves 1.3 mm depth and 2.0 mm pitch.)

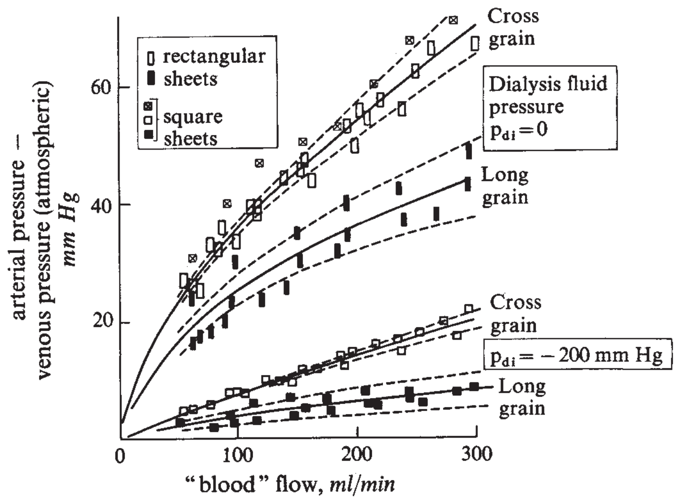

Fig. 2. *Effect of "blood" flow on blood arterial pressure.* (Venous pressure = atmospheric; dialysis fluid flow = 500 ml/min)

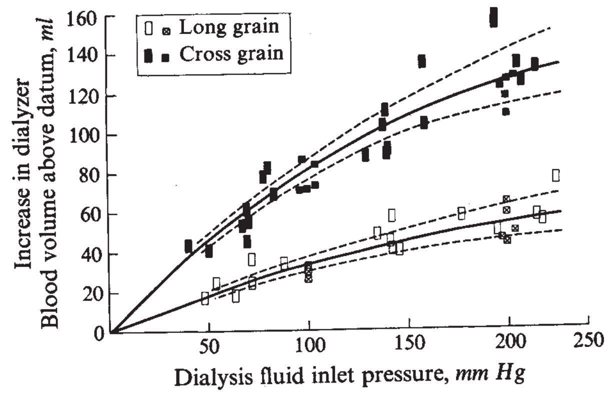

Fig. 3. *Effect of dialysis fluid inlet pressure on dialyzer "blood" volume.* (Datum values: 113 ± 11 SD ml cross grain, 131 ± 16 SD ml long grain)

assembly techniques were used, care being taken to avoid creasing and stretching by slight tensioning only along the grain direction. Using water-based solutions, simulation of *in vivo* conditions followed that recommended by Fritz [5]. Flow temperatures were kept at 37 ± 0.5° C.

The long-grain orientation required a significantly lower ($P=0.001$) arterial pressure than the cross-grain orientation (Fig. 2) for a given blood flow and venous pressure (standard error of difference = 3.8 mm Hg, student $t=3.8$, degrees of freedom $N=38$; $P_{di}=0$). Assuming Poiseuille flow, this information suggests a blood film thickness 13% larger at atmospheric dialysis fluid pressure. This difference was confirmed by the priming volume of 131 ml (SD = 16 ml) for the long grain and 113 ml (SD = 11 ml) for the cross grain, a difference which is significant at the 1% level (SED = 5.6 ml, $t=3.2$, $N=21$). On application of negative dialysis fluid pressure, the hydrodynamic resistance to blood flow reduced significantly with both orientations (Fig. 2). At the same time the long-grain membrane distended nearly three times more into the supporting grooves than the cross-grain (Fig. 3). The fairly narrow confidence limits (5%) on the means indicate that this difference between the two orientations is highly significant ($P<0.1$%). Despite these relative changes in blood film thickness, no significant difference in urea and creatinine clearance could be detected at normal clinical levels of blood flow and at atmospheric dialysis fluid pressure (Fig. 4). However (Fig. 5), the long-grain orientation produced on average a 50% higher level of ultrafiltration than the cross-grain orientation at a given transmembrane pressure (for the rectangular sheets: SED = 0.4 ml/min/100 mm Hg, $t=4.2$, $N=43$, $P=0.001$). In addition, equally significant variations of ultrafiltration, of the order of 2 to 3 ml/min/100 mm Hg, occurred with both orientations between the batches of rectangular and square sheet membranes, which were rated by the manufacturer as standard material (Fig. 5). However no significant variation between batches in any of the other characteristics could be detected. The effect of reducing the dialysis fluid pressure from atmospheric to 200 mm Hg

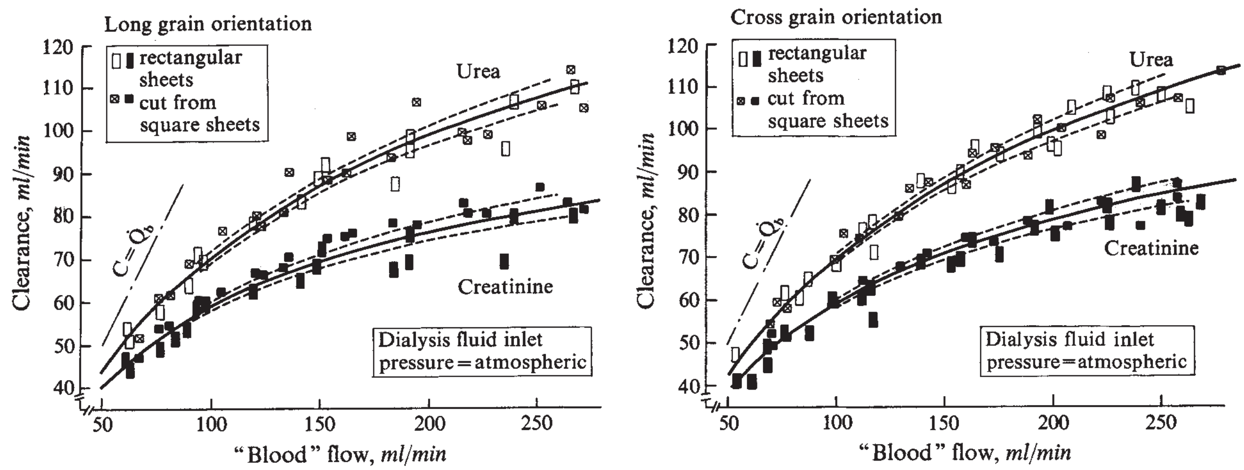

Fig. 4. *Effect of "blood" flow on urea and creatinine clearance at a dialysis fluid flow of 500 ml/min.* (Dotted lines indicate 5% confidence limits of the mean; clearance uncorrected for ultrafiltration)

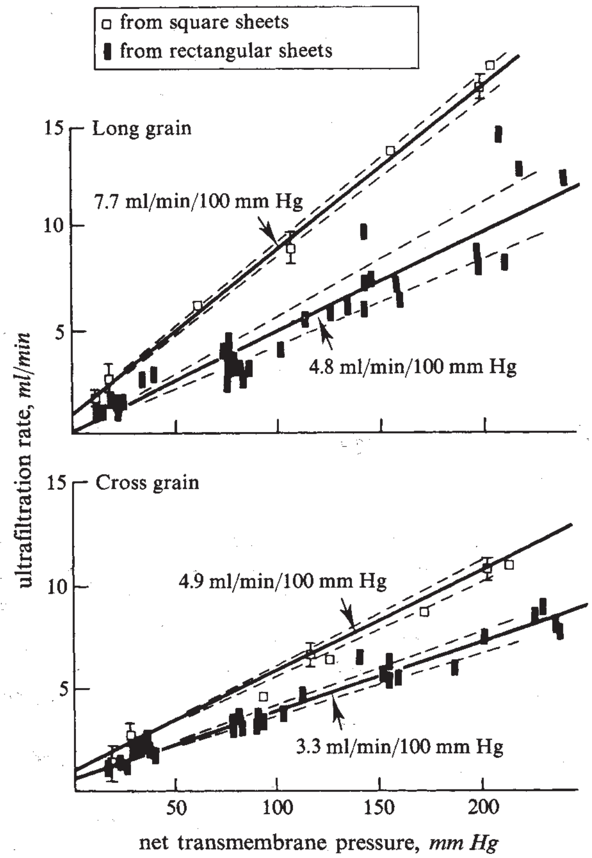

Fig. 5. *Effect of transmembrane pressure on ultrafiltration rate.* (Dotted lines indicate 5% confidence limits on the mean slope; the points indicated by ⫯ are the mean and range of five separate assemblies.)

vacuum was observed to increase the clearance of both urea and creatinine by 6% with both orientations (Table 1). In this table the calculation of clearance from the arterial and venous samples allows for the venous flow's being lower than the arterial flow because of ultrafiltration. If this correction is not made, then the clearance levels, attributable to diffusion only, show a reduction as the dialysis fluid pressure is reduced.

The general pattern of the results is consistent with increased stretching of the membrane into the membrane support when the structural grains lie parallel to the membrane support. The change in ultrafiltration characteristics is attributable to the increased molecular pore size that must inevitably occur. The result suggests that the detailed molecular structure under stress is just as important as the fluid dynamics effect of a high transmembrane pressure. The potential loss in clearance due to the increased blood film thickness and loss of surface area of the long-grain orientation must be offset by a combination of increased dialysis fluid turbulence in the thinner channel, and increased solute transfer due to the higher ultrafiltration; the latter effect only becomes significant above a transmembrane pressure of 50 mm Hg. In clinical use there must be some uncertainty in the ultrafiltration rate with

Table 1. Effect of dialysis fluid pressure (P_{di}) on clearance (Square sheet tests)

Parameters	P_{di} *mm Hg* gauge 0	−200	Change due to pressure change
Urea clearance, ml/min			
Cross grain	101 ± 3 SD	106 ± 2 SD	+5%
Long grain	102 ± 5 SD	108 ± 2 SD	+6%
Creatinine clearance, ml/min			
Cross grain	$81 \pm 2\frac{1}{2}$ SD	86 ± 2 SD	+6%
Long grain	81 ± 3 SD	86 ± 2 SD	+6%
Ultrafiltration rate, ml/min			
Cross grain	$2 \pm \frac{1}{2}$ SD	$11 \pm \frac{1}{2}$ SD	—
Long grain	$2\frac{1}{4} \pm \frac{1}{2}$ SD	$16\frac{1}{2} \pm \frac{1}{2}$ SD	—

Mean blood flow = 200 ml/min; dialysis fluid outlet flow = 500 ml/min.

Table 2. Estimated effect of grain orientation on dialyzer performance in a pumpless circuit

Performance characteristic		Mean arterial pressure[a] *100 mm Hg* XG	LG	*140 mm Hg* XG	LG
Circuit resistance[b]	*mm Hg*	28	40	48	66
Dialyzer resistance	*mm Hg*	72	60	92	74
Blood flow[c]	*ml/min*	100	140	150	205
Urea clearance	*ml/min*	69	84	87	100
Creatinine clearance	*ml/min*	59	68	70	77

[a] Venous pressure = 0 (atmospheric).
[b] Arbitrary levels, factored in direction proportion to the blood flow.
[c] Estimated from Fig. 2 assuming $p_{di} = 0$ and factoring data by 2 to allow for the greater viscosity (×3) of real blood. (Arterial pressure does *not* go up pro rata because of extra distension.)

either orientation, which could be undesirable for home-based patients. Weight change during dialysis appears to bear a predictable relationship to the applied negative pressure in some studies [6] but not in others [7]; this puzzling difference may be partly or wholly explained by variation between membrane batches and by the choice of different membrane orientations, though one cannot test this theory since the grain direction is hardly ever quoted in papers on hemodialysis. The substantial increase in priming volume with long-grain orientation when negative pressure is applied to the dialysis fluid pathway is undesirable; it is liable to cause hypotension in patients with poor vasa-motor control when fast ultrafiltration is attempted, limiting the opportunities for fluid removal. In general, the level of scatter on the various characteristics is of the same order or somewhat greater for the long-grain orientation. This implies a greater uncertainty as to the effects of each hemodialysis with long-grain membranes, compared to the cross-grain membrane. The cross-grain orientation is therefore preferable on most counts to long-grain during pumped dialysis. On the other hand, the lower resistance to blood flow with long-grain membrane is an attractive feature for pumpless dialysis with an arteriovenous shunt. The improved blood flow, and therefore clearance, that will result depends on a number of factors, in particular the blood pressure, the resistance of the shunt and the ultrafiltration required. Table 2 shows that improvements in clearance of 10 to 20% should occur; the higher the assumed blood pressure and circuit resistance, the lower the predicted improvement is. It is not certain that this would apply to molecules of higher molecular weight, since in this case the clearance tends to be limited only by effective membrane area, not by the blood or dialysis fluid flow [8]. At high transmembrane pressure this effective area should be lower for the long-grain than for the cross-grain, since the higher blood volume suggests more physical contact with a Kiil-type groove. However the pore shape, which is elliptical in the unstrained state [3], will become more circular in the long grain and even more elliptical in the cross-grain. Thus this effect will be favorable for the long-grain orientation. It has been shown [9], for instance, that the half-time life for ribonucleases across Visking tubing is significantly increased by stretch along the grain direction but is significantly lowered by stretch across the grain direction.

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